REMARKS

Claims 1-2, 7-25 are pending in this application. Claims 21-25 were withdrawn from consideration by the examiner.

ELECTION/RESTRICTIONS

The examiner alleged that newly submitted claims 21-25 are directed to an invention that is independent or distinct from the invention originally claimed. Further alleged is that the newly submitted claims 21-25 are materially distinct methods which differ in objectives, method steps, response variables, and criteria for success.

The examiner states that the original claims have been constructively elected by original presentation for prosecution on the merits. The examiner then withdrew claims 21-25 from consideration by being directed to a non-elected invention.

Applicants respectfully traverse and disagree with the examiner's conclusions regarding new claims 21-25.

There are two criteria for a proper requirement for restriction

1) inventions must be independent or distinct as claimed, and

2) there must be a serious burden on the examiner. MPEP 803.

The examiner must provide reasons and/or examples to support his/her conclusions. These requirements have not been met. MPEP 816.

Independent means there is no disclosed relationship between the subjects disclosed, *i.e.*, unconnected in design, operation, or effect. MPEP 802.01. Though claims 21-25 as presented are not dependent claims, the examiner has given no reasoning why the claimed invention is independent of the examined invention(s).

Distinct means that two or more subjects disclosed are related, but are capable of separate manufacture, use or sale as claimed, and are PATENTABLE OVER EACH OTHER. MPEP 802.01 (emphasis in original).

Further, if the search and examination of the application can be made without serious burden, the examiner **must** examine it on the merits, even though it includes claims to independent or distinct inventions. MPEP 802.01. The examiner gives no indication or reasoning of serious burden for search and examination such as separate classification, separate status in the art, or different field of search. There is no reason that different searches would be required for the new claims as opposed to the examined claims. The examiner has not established a *prima facie* case. MPEP 803. The burden of proof does not shift to Applicants until the examiner has established a *prima facie* case.

Under MPEP 821.03, claims added by amendment following action by the examiner should be treated as indicated by 37 C.F.R. 1.145. 37 C.F.R. 1.145 states that if the applicant presents claims directed to an invention distinct from **and** independent of the invention previously claimed, the applicant will be required to restrict claims to the previously claimed invention. This differs from the normal criterion 1) for restriction which only requires that the inventions be independent or distinct as claimed. The examiner has not alleged nor given reasons that the newly submitted claims were distinct **and** independent from the original claims. The examiner only asserts that the claims are directed to an invention that is independent or distinct and states that the examiner believes the inventions are "materially distinct." In fact, the Examiner does not even support the assertion that the invention is independent. Claims 21-25 have not been treated as required by 37 C.F.R. 1.145. Also, as argued above, the second criterion 2) regarding serious burden has not been established.

Claim 21 is "[a] method for substantially simultaneously visualizing epithelial origin of a cell and the chromosome count of the cell comprising, in the following order:

a. obtaining a biological sample containing a cell from a patient;

b. performing immunocytochemistry on the sample to indicate epithelial origin;

c. analyzing the stained cell for chromosomal count."

Claims 22-25 depend from claim 21.

A comparison of this claimed subject matter to the claims which were examined must be done. MPEP 806.01. The similarity between step a and step a from the examined method claims is apparent. It is also apparent that steps b and c relate to embodiments of or portions of embodiments of the steps in the examined claims (*see* specification).

Still further, the present restriction requirement has not previously been presented by the examiner, traversed by Applicants, and is now made final. Applicants believe the requirement for cancellation of the claims is premature until there has been an opportunity to traverse the requirement. MPEP 821.01. Applicants respectfully request reconsideration of this restriction requirement before such requirement is made final. *See also* MPEP 821.03/37 C.F.R. 1.145 ("subject to reconsideration and review...").

35 U.S.C. §102

WO 97/38313

Claims 1, 2, 7-15, 17 and 19 were rejected under 35 U.S.C. §102(b) as being anticipated by WO 97/38313 (IDS A2). The examiner asserts that claims 1, 2, 7-15, 17 and 19 were interpreted as being drawn to a cancer detection method by enriching circulating epithelial cells by positive selection and detecting a hybridization pattern with a probe or multiple probes using various conventional detection methods.

The examiner alleges that WO 97/38313 at Example 10 teaches a method of enriching and screening for the presence of a cancer cell from patients' blood by contacting the sample with an agent (*i.e.*, anti-cytokeratin antibody) that binds to the epithelial cells as well as detecting cancer cells using various methods known in the art such as FISH.

The Examiner also alleges that the reference further teaches a method of separating and detecting cancer cells using immunomagnetic beads and other methods known in the art (the 2nd paragraph of page 2) including the instantly claimed "positive selection," wherein a rare cell (*i.e.*, circulating cancer cell) is bound to a binding agent such as an antibody, thereby [*sic*] the bound cancer cell is separated from the non-cancer cells (especially note page 2, lines 16-18).

The Examiner also alleges that the reference further teaches detecting the hybridization pattern using various conventional detection methods (see page 21 to the first paragraph of page 26) and multiple probes (Example 7). The allegedly disclosed examples of probe associated with specific cancer and genetic marker are PSMA, PSA, and centromeric regions of chromosomes 7, 8, 18 (page 21-22). Further, the examiner alleges that WO 97/38313 teaches methods of determining status and progress of a cancer patient and monitoring efficacy of cancer treatment at page 3, lines 18-26, page 25, lines 19-26, examples 2, 7, and 11.

Applicants respectfully traverse the rejection. All of Applicants' previous arguments are repeated herein in addition to the clarifications given below.

The method of WO 97/38313 first runs a fluid sample (1) through density gradient separation. This gives a sample (2) with an increased concentration of rare non-blood cells (cancer cells/epithelial cancer cells). Sample (2) is then subjected to a "negative selection process". This entails subjecting sample (2) to an agent that binds the non-rare cells (blood cells) ("precisely the opposite of conventional processes," p. 7, line 31) rather than the rare cells (cancer cells) ("positive selection process"). The bound non-rare cells are then separated from

sample (2). Then, the rare cells can be further processed, such as by identification, characterization and/or culturing. Embodiments of the methods are asserted to provide improved diagnosis, staging, and monitoring of cancer in a patient.

The methods of the present invention include positive detection and selection processes. Enrichment is via binding of the cancer cell rather than the non-rare blood cells.

Example 10 states that it discloses identification of LNCaP cells or prostatic cancer cells from patients' blood by the combination of immunocytochemistry stain with cytokeratin mAb, FISH with chromosomal centromere 7 and 18 probes, and PSMA mRNA probe. The example states that "the sample is fixed" but does not say what "the sample" includes or how it was prepared. The other examples explicitly say how the sample is prepared. Example 10 appears to be the only example which does not specify the sample. The stained samples were examined under a fluorescent microscope for "percentage of positive staining." Since the samples are spiked, it is known that cancer cells are present, but it is not disclosed (taught) in this example what, if any, other cells are present in the samples. Therefore, even if the cancer cells can be "positively" identified, there is no positive selection or enrichment for those cancer cells. Identification is different than enrichment.

Claim 1 step a of the present application is "obtaining a cell from biological sample comprising a cell from a subject, wherein the sample is enriched for circulating epithelial cells by an agent binding with the epithelial cells." This step includes a **"positive"** selection (binding with the epithelial cells) **enrichment**, therefore, WO 97/38313 cannot anticipate claim 1. Example 10 does not, nor the rest of the reference, as the examiner alleges, disclose "**enrich[ing]** for circulating epithelial cells by contacting the sample with an agent that binds with the epithelial cells." The specified agents of Example 10 do not serve to enrich the sample(s), but instead only stain the samples. The staining of the samples is solely for identification, and no

enrichment of the sample is disclosed. Further, as discussed below for Racila *et al.*, cytokeratin staining does not distinguish a non-cancer cell from a cancer cell, but instead may only identify an epithelial cell. Additionally, WO 97/38313 as a whole discloses that "positive selection" processes exist (conventional processes) (p. 2, lines 5-25), however, WO 97/38313 does not itself teach or use such a method. WO 97/38313 by itself does not enable a positive selection process. MPEP 2121 *et seq.*

Claims 2, 7-13 depend from claim 1, thus, these claims also cannot be anticipated.

Claim 7 comprises enrichment for circulating epithelial cells by cytokeratin "screening." There is no enrichment for circulating epithelial cells disclosed in WO 97/38313. The use of cytokeratin staining in Example 10 indicates the presence of epithelial cells (spiked cancer cells) but performs no enrichment. It further appears that the examiner is incorrectly construing cytokeratin "staining" and cytokeratin "screening" to be the same thing. "Staining" alone does not "enrich" a sample.

Claim 14 includes in step a the limitation " a biological sample compris[ing] a mixed cell population suspected of containing a population of epithelial cells...." It is not disclosed in Example 10 whether a mixed cell population is used, and if so, whether the sample is suspected to contain epithelial cells. Claim 14 comprises step b: "mixing the biological sample with magnetic particles coupled to a ligand which is capable of reacting specifically with epithelial cells to the substantial exclusion of non-epithelial cells." The disclosed ligands bound to magnetic particles in WO 97/38313 bind to primary antibodies (p. 4, lines 28-30) or to non-rare cells (p. 16-18), not to epithelial cells. Therefore, step b is clearly missing from WO 97/38313 and, thus, WO 97/38313 cannot anticipate this claim. The Background of WO 97/38313 discloses that methods of separating and detecting cancer cells which use immunomagnetic beads exist (*e.g.*, p. 2, line 6) (p. 2, lines 5-25), however, WO 97/38313 does not itself teach or

use (enable) such a method for positive selection/enrichment. Line 6 of page 2 of the cited reference does not specify that the "ligand ... react[s] with epithelial cells ...," instead it makes no mention of a ligand on a bead or what a ligand may or may not bind. Additionally, WO 97/38313 does not itself teach or use a method with step c (enriching . . . for epithelial cells . . .), nor do the lines on page 2 of the cited reference disclose this step.

Claim 15 comprises step b: "enriching the sample for circulating epithelial cells by an agent binding with the epithelial cells." This step includes a positive selection enrichment as discussed in detail above for the previous claims, therefore, WO 97/38313 cannot anticipate claim 15. **Further**, claim 15 includes step e: "determining the amount of cancer cells... and correlating the amount of cancer cells...with a stage of cancer, ..." WO 97/38313 states that it teaches methods of determining status and progress of cancer patient and monitoring efficacy of cancer treatment at page 3, lines 18-26, page 25, lines 19-26, examples 2, 7, and 11. **However**, the reference does not enable methods of determining status and progress or monitoring efficacy of treatment. WO 97/38313 does not teach, *e.g*, counting, determining the amount of cancer cells **and** correlating the amount with the stage of cancer. Example 2 teaches what percentage spiked cells were recovered from samples using a gradient column. Example 7 takes isolated cancer cells and adds oligonucleotide probes and counts stained chromosomal centromeres, but does not disclose counting cancer cells. Example 11 uses the procedure of sample 2 to isolate prostate cancer cells from blood of "advanced" prostate cancer patients. Example 11 may determine the amount of cancer cells in a given sample but **does not correlate** the amount of cells in the sample with a stage of cancer. Example 11 patients all had the same stage of cancer, as classified in the example.

Claim 17 comprises step b: "enriching the first and second samples for circulating epithelial cells by an agent binding with the epithelial cells." This step describes a positive

selection enrichment, therefore, as discussed in detail above for the previous claims, WO 97/38313 cannot anticipate claim 17. **Further**, claim 17 comprises step e: "determining the amount of cancer cells...[in a first and second sample]" and step f: "comparing the amount of cancer cells...[in the first and second sample], whereby the relative amount[s]...may be correlated with the progression of cancer...." WO 97/38313, as discussed in detail for claim 15, does not disclose or teach comparing multiple samples for relative amounts of cancer cells **and correlating** with the progression of cancer.

Claim 19 comprises step b: "enriching the sample for circulating epithelial cells by an agent binding with the epithelial cells." This step describes a positive selection enrichment, therefore, as discussed in detail above for the previous claims, WO 97/38313 cannot anticipate claim 19. **Further**, claim 19 comprises step e: "determining the amount of cancer cells... and correlating the amount of cancer cells...with the effectiveness of an anti-cancer treatment." WO 97/38313, as discussed in detail above for claim 15, does not disclose or teach **correlating** the amount of cancer cells with effectiveness of anti-cancer treatment.

These rejections should now be overcome.

Racila *et al.* (April 1998)

Claims 16, 18, and 20 were rejected under 35 U.S.C. §102(a) as being anticipated by Racila *et al.* (IDS A26).

The examiner asserts that the previous arguments regarding the missing limitation "detection of the complex can distinguish a non-cancer cell from a cancer cell" were not found to be persuasive. The examiner asserts that the arguments were not persuasive because the reference allegedly teaches that the complex formed in Racila *et al.* (*i.e.*, anti-cytokeratin and

cytokeratin complex, and anti-mucin and mucin complex) is indicative of cancer cells (note abstract) (emphasis added).

Applicants respectfully traverse the rejection. The complex formed in Racila *et al.* (*i.e.*, anti-cytokeratin and cytokeratin complex and anti-mucin and mucin complex) is clearly taught in the body of Racila *et al.* to be indicative of epithelial cells **not** cancer cells (note abstract and throughout reference, specific passages noted below).

Also, it appears that the examiner is construing the claim limitation "distinguish" to mean detection of the complex is "indicative" of cancer cells. The examiner's definition of "indicative" appears to broadly mean some correlation is believed to or might exist between the presence of the complex and the presence of a cancer cell. By Applicants distinguishing Racila in the specification, it is clear that the "detection of the complex can distinguish a non-cancer cell from a cancer cell" limitation is to be construed to not include the subject matter of Racila. Therefore, the examiner's construction of "distinguish" is incorrect.

Further, it is the "detection of the complex" that distinguishes the status of the cell, not another step. In Racila, a step of correlation with another assay (*e.g.*, "morphology" or "and cytological evidence") or a step of assaying (*e.g.*, morphology) is necessary to "distinguish a non-cancer cell from a cancer cell." At best, Racila *et al.* characterized their own immunocytochemistry results as "suggestive" (p. 4593) and "may" allow predictions (p. 4593). Applicants draw the examiner's attention particularly to the last column of Racila on p. 4593, more particularly to the first full paragraph of that column beginning with "[a]lthough the assay described here..."

The following clarifies (for example, using additional specific quotations from Racila) the Applicants' previous arguments for the examiner that Racila is indeed missing the limitations found in the rejected claims of the present application.

As pointed out on p. 29, lines 10-13 of the present application, in reference to the method taught by Racila (emphasis added), "[t]his procedure has the capacity to detect whether epithelial cells are present in a sample, such as blood, but does not indicate the genetic status of the cells detected. Therefore further assays on the same sample are required to determine more conclusively the genetic status [*i.e.*, cancer status] of these epithelial cells." The circulating epithelial cells of Racila *et al.* were simply **assumed** to be tumor cells. The malignant nature of the cells was demonstrated by their cytology **and** immunophenotype, not by them being epithelial cells.

The elements in the cell suspension of Racila *et al.* were tagged using a second mAb specific for cytokeratin (mAb specific for a molecule on epithelial cells), a third mAb against a pan leukocyte antigen (CD45), and a nucleic acid dye **to** "allow exclusion of residual red blood cells and other nonnucleated events" (p. 4590, Results, lines 15-19 emphasis added). The antibodies CD45 and cytokeratin only identify the cells as epithelial or non-epithelial based on the positive or negative staining of the cells viewed, not as to whether the cells are cancerous. Note for example the abstract, "[p]eripheral blood... was examined ... for the presence of circulating **epithelial cells defined** as nucleic acid+, CD45-, and cytokeratin+" (emphasis added). This clearly shows that reaction with these three reactants only demonstrates presence of epithelial cell markers.

It is known to those of ordinary skill in the art that presence of epithelial cells does not correlate 100% to cancer cells. Presence of circulating epithelial cells can indicate other reasons for the presence of the cells. For example, see Table 1 of Racila—7 donors of 13 healthy control donors had circulating epithelial cells identified by flow cytometry (*i.e.*, the portion of the assay involving staining with mAb specific for cytokeratin, mAb against a pan leukocyte antigen (CD45), and a nucleic acid dye); Racila *et al.* also had not tested the blood of patients with non-

malignant diseases to determine whether the assay could be used to distinguish from carcinoma cells -- further clarifying that the presence of epithelial cells was only assumed to indicate cancer status whereas the further assays were needed to show that they were cancerous (p. 4593, second column, first full paragraph).

The abstract generalizes that the assay for cancer cells is a combination of the methods used, not simply the antibody staining. As accurately stated in the abstract, "[t]o determine whether the circulating epithelial cells in the cancer patients were neoplastic cells, ..." further analyses were required (emphasis added). Also, *see* p. 4589, top of the second column, line 5: "The malignant nature of the cells was demonstrated by their cytology and immunophenotype." To examine whether the cells identified as epithelial cells by flow cytometry could be classified as tumor cells, the cells were subjected to the immunomagnetic sample preparation followed by a cytospin that allows cells to be studied for morphology and additional markers. "To examine whether the cells identified as epithelial cells by flow cytometry [*i.e.*, staining with mAb specific for cytokeratin, mAb against a pan leukocyte antigen (CD45), and a nucleic acid dye] could be classified as tumor cells, ... This procedure allows individual cells to be studied for morphology and additional markers, ..." (p. 4591, 2nd full paragraph, emphasis added).

Claim 16 is not anticipated. The complex formed in Racila *et al.* was only used to indicate identification of epithelial cells, thus, the limitation "detection of the complex can distinguish a non-cancer cell from a cancer cell" in step c is not met. The whole two step assay of Racila, may or may not distinguish a non-cancer cell from a cancer cell, but it is clear that the "detection of the complex" step in Racila did not distinguish between cancer and non-cancer.

Further, the limitations found in steps d and e of claim 16 are not present in Racila, *i.e.*, "determining the amount of cancer cells in the sample" and "correlating the amount of cancer cells in the sample with a stage of cancer." Racila determined the amount of epithelial cells in

the sample and attempted to correlate blood levels of epithelial cells with changes in clinical status. There was no correlation (or even determination) of the amount of cancer cells with the stage of cancer. There was no second step to the Racila assay with the cancer patients of Figure 4 to determine if the epithelial cells found in the blood were cancerous or non-cancerous epithelial cells, thus the "amount of cancer cells" was unknown in these samples. One of skill in the art would know that at least some of the epithelial cells were non-cancer cells (though this is apparent from the reference by itself as well without resort to knowledge of one of skill in the art).

Claim 18 is also not anticipated. The limitation "detection of the complex can distinguish a non-cancer cell from a cancer cell" in step c of claim 18, like the limitation of claim 16, is missing, as Racila's complex (immunostaining) only distinguishes between epithelial and non-epithelial, not non-cancer from cancer.

Further, like claim 16, the limitations found in steps d and e of claim 18 are not present in Racila, *i.e.*, "determining the amount of cancer cells in the first sample and the second sample" and "comparing the amount of cancer cells in both the first sample and the second sample, whereby the relative amount of cancer cells in the first sample as compared with the second sample may be correlated with the progression of cancer...." Racila determined the amount of epithelial cells in the samples over time and attempted to correlate blood levels of epithelial cells with changes in clinical status. There was no correlation (or even determination) of the amount of cancer cells with the stage of cancer. There was no second step to the Racila assay with the cancer patients of Figure 4 to determine if the epithelial cells found in the blood were cancerous or non-cancerous epithelial cells, thus the "amount of cancer cells" was unknown in these samples. One of skill in the art would know that at least some of the epithelial cells were non-cancer cells.

Claim 20 is not anticipated. As discussed above for claims 16 and 18, the limitation of "detecting the complex can distinguish a non-cancer cell from a cancer cell" in step c of claim 20, is missing, as Racila's complex (immunostaining) only distinguishes between epithelial and non-epithelial, not non-cancer from cancer.

Further, the limitation found in step d of claim 20 is not present in Racila, *i.e.*, "determining the amount of cancer cells in the sample and correlating the amount of cancer cells in the sample with the effectiveness of the anti-cancer treatment ...." Racila *et al.* determined the amount of epithelial cells in samples over time and attempted to correlate blood levels of epithelial cells with changes in clinical status. There was no correlation (or even determination) of the amount of cancer cells with the stage of cancer or the effectiveness of anti-cancer treatment. There was no second step to the Racila assay with the cancer patients of Figure 4 to determine if the epithelial cells found in the blood were cancerous or non-cancerous epithelial cells, thus the "amount of cancer cells" was unknown in these samples. One of skill in the art would know that at least some of the epithelial cells were non-cancer cells.

This rejection should now be withdrawn.

Attached hereto is a marked-up version of the changes made to the specification and claims. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

The undersigned believes that no extension of time is necessary to make this response timely. This amount is believed to be correct. Should this be in error, Applicants respectfully

requests that the Office grant such time extension pursuant to 37 C.F.R. § 1.136(a) as necessary to make this Reply timely, and hereby authorizes the Office to charge any necessary fee or surcharge with respect to said time extension or any additional fees which may be required, or credit any overpayment to the deposit account of the undersigned firm of attorneys, Deposit Account 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8

I hereby certify that this document and any documents referenced herein as being enclosed herein is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Patricia L. Ades — Date Apr 15, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

NOTE: ALL CLAIMS ARE INCLUDED FOR THE CONVENIENCE OF THE EXAMINER WHETHER THEY HAVE BEEN AMENDED OR NOT.

IN THE SPECIFICATION

No changes.

IN THE CLAIMS

No changes.

1. A method of screening for the presence of a cancer cell, comprising:
   a. obtaining a cell from a biological sample comprising a cell from a subject, wherein the sample is enriched for circulating epithelial cells by contacting the sample with an agent that binds with the epithelial cells;
   b. contacting the cell with a probe capable of hybridizing to a nucleic acid of the cell; and
   c. detecting the hybridization pattern of the probe, whereby the hybridization pattern can distinguish a non-cancer cell from a cancer cell, thereby screening for the presence of a cancer cell.

2. The method of claim 1, wherein the cell is a tumor cell.

7. The method of claim 1, wherein the enrichment of the sample for circulating epithelial cells is achieved by cytokeratin screening.

8. The method of claim 1, wherein the probe is associated with a specific cancer, thereby identifying the organ-origin of the cancer cell.

9. The method of claim 1, wherein the probe is specific for a genetic marker.

10. The method of claim 1, wherein the probe is associated with a chromogenic dye.

11. The method of claim 1, wherein the probe is associated with a fluorescent dye.

12. The method of claim 1, wherein detection comprises spectral imaging.

13. The method of claim 1, wherein detection comprises utilizing multiple probes.

14. A method of screening for the presence of a cancer cell, comprising:
    a. obtaining a biological sample from a subject, wherein the biological sample comprises a mixed cell population suspected of containing a population of epithelial cells which include a cancer cell;
    b. mixing the biological sample with magnetic particles coupled to a ligand which is capable of reacting specifically with epithelial cells to the substantial exclusion of non-epithelial cells;
    c. enriching the biological sample for epithelial cells by subjecting the cells of step b to a magnetic field to produce a cell suspension that is enriched epithelial cells;
    d. contacting the cells of step c with a probe capable of hybridizing to nucleic acid of the cell; and
    e. detecting the hybridization pattern of the probe, whereby the hybridization pattern can distinguish a non-cancer cell from a cancer cell, thereby screening for the presence of a cancer cell.

15. A method of determining the status of a cancer comprising:
    a. obtaining a biological sample containing a cell from a patient diagnosed with cancer;
    b. enriching the sample for circulating epithelial cells by contacting the sample with an agent that binds with the epithelial cells;

c. contacting the cell in the enriched sample with a probe capable of hybridizing to nucleic acid of the cell;

d. detecting the hybridization pattern of the probe, whereby the hybridization pattern can distinguish a non-cancer cell from a cancer cell;

e. determining the amount of cancer cells in the enriched sample and correlating the amount of cancer cells in the enriched sample with a stage of cancer, thereby determining the status of the cancer.

16. A method of determining the status of a cancer comprising:

a. obtaining a biological sample containing a cell from a patient diagnosed with cancer;

b. contacting the cell in the sample with a probe under conditions capable of forming a complex with an antigen of the cell;

c. detecting the complex, whereby detection of the complex can distinguish a non-cancer cell from a cancer cell;

d. determining the amount of cancer cells in the sample; and

e. correlating the amount of cancer cells in the sample with a stage of cancer, thereby determining the status of the cancer.

17. A method of determining the progression of a cancer comprising:

a. obtaining a biological sample containing a cell at a first time point from a patient diagnosed with cancer and obtaining a biological sample containing a cell from the patient at a second time point;

b. enriching the first and second samples for circulating epithelial cells by contacting the samples with an agent that binds with the epithelial cells;

c. contacting the cell in the first enriched sample and the cell in the second enriched sample with a probe capable of hybridizing to nucleic acid of the cell;

d. detecting the hybridization pattern of the probe, whereby the hybridization pattern can distinguish a non-cancer cell from a cancer cell;

e. determining the amount of cancer cells in both the first enriched sample and the second enriched sample; and

f. comparing the amount of cancer cells in both the first enriched sample and the second enriched sample, whereby the relative amount of cancer cells in the first enriched sample as compared with the second enriched sample may be correlated with the progression of cancer, thereby determining the progression of the cancer.

18. A method of determining the progression of a cancer comprising:

a. obtaining a biological sample containing a cell at a first time point from a patient diagnosed with cancer and obtaining a biological sample containing a cell from the patient at a second time point;

b. contacting the cell in the first sample and the cell in the second sample with a probe under conditions which allow the probe to form a complex with an antigen of the cell;

c. detecting the complex in both the first sample and the second sample, whereby detection of the complex can distinguish a non-cancer cell from a cancer cell;

d. determining the amount of cancer cells in the first sample and the second sample; and

e. comparing the amount of cancer cells in both the first sample and the second sample, whereby the relative amount of cancer cells in the first sample as compared with the second sample may be correlated with the progression of cancer, thereby determining the progression of the cancer.

19. A method of determining the effectiveness of an anti-cancer treatment comprising:

a. obtaining a biological sample containing a cell from a patient that has been administered an anti-cancer treatment;

b. enriching the sample for circulating epithelial cells by contacting the sample with an agent that binds with the epithelial cells;

c. contacting the cell in the enriched sample with a probe capable of hybridizing to nucleic acid of the cell;

d. detecting the hybridization pattern of the probe, whereby the hybridization pattern can distinguish a non-cancer cell from a cancer cell;

e. determining the amount of cancer cells in the enriched sample and correlating the amount of cancer cells in the sample with the effectiveness of the anti-cancer treatment, thereby determining the determining the effectiveness of an anti-cancer treatment.

20. A method of determining the effectiveness of an anti-cancer treatment comprising:

a. obtaining a biological sample containing a cell from a patient that has been administered an anti-cancer treatment;

b. contacting the cell in the sample with a probe under conditions capable of forming a complex with an antigen of the cell;

c. detecting the complex, whereby detecting the complex can distinguish a non-cancer cell from a cancer cell;

d. determining the amount of cancer cells in the sample and correlating the amount of cancer cells in the sample with the effectiveness of the anti-cancer treatment, thereby determining the determining the effectiveness of an anti-cancer treatment.

21. A method for substantially simultaneously visualizing epithelial origin of a cell and the chromosome count of the cell comprising, in the following order:

a. obtaining a biological sample containing a cell from a patient;

b. performing immunocytochemistry on the sample to indicate epithelial origin;

c. analyzing the stained cell for chromosomal count.

22. The method of claim 21 wherein performing immunochemistry on the sample to indicate epithelial origin is treating the sample with a labeled antibody against cytokeratin.

23. The method of claim 21 wherein analyzing the stained cell for chromosomal count is performing FISH analysis on the sample.

24. The method of claim 1 wherein the biological sample is blood.

25. The method of claim 1 whereby the hybridization pattern distinguishes a non-cancer cell from a cancer cell by detection of chromosomal aneuploidy specific for cancer.